Remarks

Claims 14-59 are pending in the subject application. Applicants gratefully acknowledge the Examiner's indication in the August 12, 2004 Office Action of the withdrawal of the rejections under 35 USC §112, second paragraph, and certain of the previous rejections under 35 USC §102. By this Amendment, Applicants have amended claims 14-20, 23, 26-28, 30, 31, 34, 37, 39, 40, 44, 48-50, 52, and 56 and canceled claims 22, 29, 33, 38, 47, and 59. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 14-21, 23-28, 30-32, 34-37, 39-46, and 48-58 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

In Section 2 of the Advisory Action dated January 11, 2005, the Examiner indicates that Applicant's Amendment submitted November 8, 2004 would not be entered because it raises new issues that would require further consideration and/or search and raises the issue of new matter. However, Applicants gratefully acknowledge the Examiner's indication in the Advisory Action that previously pending rejections under 35 USC §112 would be overcome by the amendments presented in Applicants' November 8 Amendment. Accordingly, the amendments and remarks presented herein are essentially the same as in the November 8 Amendment, with the main difference being some additional remarks regarding the amendments to claims 30, 40, and 48 (along with a change in the amendment to claim 48).

In the Advisory Action, the Examiner also indicated that all dependent claims would require examination for consistency with language in the independent claims. In particular, the Examiner indicated that the recitation in claims 30 and 40 of a "net negative charge" may be inconsistent with the presence of a polyphenol polymer as recited in independent claims 26 and 37. Applicants respectfully assert that the language in claims 30 and 40 is not inconsistent with a polyphenol polymer. It is well known in the art that polyphenol polymers can be neutral or have a net negative charge. Depending on how they are prepared, a polyphenol polymer can be made more negatively charged or less negatively charged. Accordingly, Applicants respectfully assert that the language of dependent claims 30 and 40 is consistent with the language of the claims from which they depend.

Claims 14-59 are rejected under 35 USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully assert that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention. Applicants will address each of the separate rejections below.

Under this rejection, the Examiner asserts that the subject specification does not support claims 14 and 26 directed to an immunomatrix having two polymers, each of which have a different antibody. By this Amendment, Applicants have amended independent claims 14 and 26 to indicate that the immunopolymer matrix comprises first and second immunopolymer layers, *i.e.*, the matrix comprises distinct and separate layers of immunopolymers. The Examiner acknowledges in the instant Action that there is support for such layers at pages 11-12 of the specification, noting that "each of the different antibodies is provided in a different layer of the immunomatrix." In addition, the Examiner asserts that there is no support in the specification for HRP and GOX enzymes "attached" to the polymers. Applicants have amended claims 14 and 26 to delete reference to the phrase "attached to".

Claims 14, 26, 39, and 52 are rejected as having new matter in their recitation that the antigen binding regions of the antibodies are "presented external to the surface of the immunopolymer." Applicants respectfully assert that only those Fc receptor molecules that are oriented in the polymer with their Fc binding region presented external to the polymer (*i.e.*, facing away from the internal region of the polymer) can bind the Fc region of an antibody. Those Fc receptors that are oriented within the polymer such that the Fc binding region is within the polymer itself will not be able to bind an Fc region of an antibody. This is inherent in the production of the claimed immunopolymer matrix and would be understood to be as such by an ordinarily skilled artisan having the benefit of the teachings of the subject specification. Thus, it is a natural outcome of preparing of the claimed polymers of the immunopolymer matrix that antibodies bound to the Fc receptor present in the polymer will have the antigen binding region of the antibody presented external to the surface of the polymer. However, in order to expedite prosecution of the application to completion, Applicants have amended the claims to delete the language. Accordingly, this rejection is moot.

The Examiner asserts that reference to "polythiophene" polymers constitutes a new subgene not supported by the subject specification. The Examiner also asserts that reference to "naphthalene-doped" and "toluene-doped" polypyrrole constitutes new matter. By this Amendment, claims 17 and 49 have been amended to recite "an alkyl substituted polythiophene." In addition, claims 18 and 50 have been amended to indicate that the polymer is "naphthalene sulfonate-doped" and "**p**-toluene sulfonate-doped" polypyrrole.

Claims 21, 22, 32, 33, 46, 47, 58, and 59 are rejected on the grounds that there is no support provided for an Fc receptor that binds specifically to IgA or IgG. Applicants respectfully assert that there is support for the claims. However, by this Amendment, Applicants have canceled claims 22, 33, 47, and 59 which recite that the Fc receptor binds IgA. In regard to claims 21,32, 46, and 58, Applicants assert that support for Fc receptor that binds IgG can be found, for example, at page 10, lines 17-18, which disclose Protein G. Protein G is an Fc receptor that binds IgG.

Claims 23 and 34 are rejected on the grounds that the term "sequentially oriented with respect to each other" lacks literal support in the subject specification. As noted above, claims 14 and 26 have been amended to recite that the matrix comprises separate first and second layers. As the Examiner notes, the subject specification, at pages 11-12, discloses different sequential layers of polymer that may be provided with antibodies of different specificities.

Claims 24, 25, 35, and 36 are rejected as lacking support for immunopolymer binding to an antigen not expressed on a rare cell, and another immunopolymer binding to an antigen that is expressed on a rare cell. Applicants respectfully assert there is support for the claimed subject matter. The Examiner's attention is respectfully directed to Examples 4 and 5 of the subject specification which discloses selection of <u>rare</u> $CD34^+$ $CD19^-$ cells from excess of (*i.e.*, not rare) $CD34^-$ cells using anti-CD34 antibody and anti-CD19 antibody.

Claims 26 and 37, and dependent claims 27, 28, 30-36, and 39-47, are rejected on the grounds that there is no support for polymers recited as "polyaromatic" polymers in the claims. By this Amendment, Applicants have amended claims 26 and 37 to replace "polyaromatic" with "polyphenol." The Examiner acknowledges in the Office Action that there is support for "polyphenol" polymers in the subject specification.

Claims 37 and 48, and claims dependent therefrom, are rejected on the grounds that they contain new matter in reciting an immunopolymer matrix having an Fc receptor with no antibody bound thereto. The Examiner acknowledges in the Office Action that the disclosure at page 10, lines 13-18, of the subject specification discloses this subject matter but asserts that the disclosure pertains to an "intermediate" and that this "intermediate" was not contemplated as being the invention. Applicants respectfully assert that there is no requirement under the patent statute or Patent Office rules that an applicant for patent can only claim in an application that subject matter which the application "contemplates as being the invention." An applicant is entitled to claim anything or any embodiment for which the subject specification provides written description and enablement under 35 USC §112, first paragraph. Applicants respectfully assert that both aspects of 35 USC §112, first paragraph, are satisfied for claims 37 and 48. Accordingly, Applicants respectfully assert that the subject matter of claims 37 and 48 is not new matter.

In view of the above remarks and amendments, reconsideration and withdrawal of the rejection under 35 USC §112, first paragraph, is respectfully requested.

Claims 22, 33, 47, and 59 are rejected under 35 USC §112, first paragraph, as nonenabled by the subject specification. The Examiner asserts that the specification does not enable an Fc receptor that specifically binds the Fc portion of IgA. Applicants respectfully assert that the claims are enabled by the subject specification. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §112, first paragraph, is respectfully requested.

Claims 14-37, 39, 41, 42, and 52-54 are rejected under 35 USC §112, first paragraph, as nonenabled by the subject specification. The Examiner asserts that the specification does not enable the making of an immunopolymer matrix having entrapped Fc receptors with antibody bound thereto such that the antigen binding region of the antibody is presented external to the surface of the conductive immunopolymer matrix. The Examiner argues that there is no teaching of a preferential orientation of the Fc receptors within the matrix. Applicants respectfully assert that the claims are enabled by the subject specification. Only those Fc receptors that are oriented in the polymer with the Fc binding region external to the surface of the polymer can bind the Fc region of an antibody. Those Fc receptors that are oriented with the binding region within the polymer itself will not be able to bind an Fc region of an antibody. This is inherent in the production of the immunopolymer matrix

and would be understood by an ordinarily skilled artisan having the benefit of the teachings of the subject specification. Thus, it is a natural property of the claimed invention that antibodies bound to the Fc receptor present in the polymer will have the antigen binding region of the antibody presented external to the surface of the polymer. Applicants have attached with this Amendment (and labeled as Exhibit A) a diagram illustrating this property. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §112, first paragraph, is respectfully requested.

Claims 24, 25, 35, and 36 are rejected under 35 USC §101 and under 35 USC §112, first paragraph, on the grounds the claimed invention is not supported by a well-established utility and not enabled. The Examiner also indicates that there is an issue of new matter since the paragraph spanning pages 11-12 fails to mention any "rare" cell. Applicants respectfully assert that the claimed invention has substantial utility and, therefore, is enabled. The rejected claims recite that there are two layers: one for "positive" selection and one for "negative" selection. Applicants respectfully assert that the paragraph cited by the Examiner which spans pages 11-12 is sufficient to teach this aspect of the instant invention in combination with supporting aspects taught elsewhere in the specification (see, for example, Examples 4 and 5) and that the specification supports both a substantial asserted utility and a well-established utility. The applicants also respectfully assert that the use of the terms "negative" and" positive" may have created some confusion.

The subject specification teaches how to entrap antibodies, whether to rare cell antigens (*e.g.*, CD34 on stem cells) or to antigens found on mature cells (*e.g.*, CD3, CD4, *etc.*). The specification further teaches to "simultaneously and/or sequentially collect and fractionate various cell types." In this embodiment, "antibodies to various cell types," *i.e.*, "multiple antibodies with differing specificities," such as CD34, CD3, CD4, *etc.* are "localized in different layers of a multiple layer polymeric matrix." The invention is further taught in two ways. Firstly, all the different cell types (rare and non-rare) can be bound at once, then "each type of cell" can be released "at a separate time," *i.e.*, "sequentially" by applying current to "the different layers" in such a way asto "release each type of cell at a different time." This necessarily results in the "purification and separation of these cells," *i.e.*, the end result would be that each cell type was separately selected. However, the ultimate disposition of each cell type is what determines if the selection procedure in general was positive or negative. As the Examiner suggests, one would simply discard the cells bound by

antibodies to "non-rare" antigens. This would be "negative" selection. Secondly, the same mixture of cells can be applied and bound in the same manner to the same "multiple layer polymeric matrix" bearing "multiple antibodies with differing specificities," only in this embodiment, the "T cells, NK cells, B cells, and others" can be "removed," which is another way of saying negatively selected, "simultaneously." In this embodiment, no release of the cells bound by antibodies to non-rare antigens is contemplated or stated. The cells bound to rare antigens would in this way be "positively" selected.

Further, the specification supports a well-established utility. The applicants agree with the Examiner in the statement that "in negative selection methods, one binds cells with antibodies to the "non-rare antigen." In this sense, and as is taught in the subject specification, the unwanted as well as the wanted cells must be bound, or "positively" selected. It is simply the disposition of the "positively selected" cells that determines whether they were ultimately positively or negatively selected. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §§101 and 112, first paragraph, is respectfully requested.

Claims 48, 49, 51, and 58 are rejected under 35 USC §102(b) as anticipated by Wallace *et al.* (WO 96/04340). The Examiner indicates that the process of polymerization in the Wallace *et al.* reference is not different than that of the claimed invention. The Examiner also asserts that Wallace *et al.* disclose monocytes and macrophage incorporated in the polymer and that such cells inherently bear Fc receptors. Thus, the Examiner concludes that all elements of the rejected claims are taught by the Wallace *et al.* reference. Applicants respectfully traverse this grounds of rejection.

Applicants respectfully assert that the Wallace *et al.* reference does not teach or suggest the claimed invention. In the Advisory Action dated January 11, 2005, the Examiner indicated that the amendment to claim 48 submitted in Applicants' Amendment dated November 8, 2004, to have it recite that the molecule having specificity for a target molecule is "non-cell bound," may constitute new matter by a negative limitation. Applicants respectfully assert that the "non-cell bound" language is not new matter. It can be understood from the specification that Applicants intended that in one embodiment the polymer matrix can have free molecules that were not part of a cell immobilized in the polymer, *i.e.*, an embodiment wherein molecules, and not cells, are embedded in the polymer. It is well settled in patent law that the claim language of an amendment need not be

disclosed word for word in a specification. *In re Wilder*, 222 USPQ 369, 372 (Fed. Cir. 1984) ("It is not necessary that the claimed subject matter be described identically, but the disclosure must convey to those skilled in the art that applicant had invented the subject matter later claimed.") (emphasis added). Thus, Applicants respectfully assert that the "non-cell bound" language is supported by the subject specification and, therefore, does not constitute new matter. However, in order to clarify that the molecule of the claim (an Fc receptor) is not part of a cell and in order to expedite prosecution of the application to completion, Applicants have amended claim 48 to recite that the molecule having binding specificity is a "cell-free" molecule. Support for the amendment can be found, for example, at page 11, lines 11-16, of the subject specification which discloses incorporation of molecules, not cell-bound or cell-associated, into the polymer. Applicants respectfully assert that, as noted above, the disclosure of the subject specification clearly contemplates that the "molecule" within the polymer is a cell-free molecule. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §102(b) is respectfully requested.

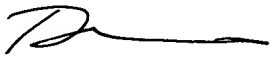
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Doran R. Pace
Patent Attorney
Registration No. 38,261
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

DRP/sl